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## ON THE ALTERATIONS INDUCED BY INTERMITTENT FEVER IN THE PHYSICAL AND CHEMICAL QUALITIES OF THE URINE, AND ON THE ACTION OF THE DISULPHATE OF QUININE.

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WE know but little at present concerning the modifications produced by diseases in the function of regressive metamorphosis of tissue, and yet it is very obvious that here our observations, if properly directed, can hardly fail to lead to results of very great importance. The exhalations from the skin and lungs, the urine, and the feces, are so many points upon which to concentrate our efforts; and by carefully studying these several excretions, a vast amount of knowledge may be obtained relative to the pathological actions going on within the system. The facility and exactness with which such inquiries can be prosecuted is only beginning to be perceived, and a rich harvest is reserved for those who will devote themselves to this field of labor.

The condition of the urine in intermittent fever has been observed by Becquerel,<sup>1</sup> and more recently by Stuart<sup>2</sup> and others. Becquerel's investigations are of the most limited character, being confined to the determination of the specific gravity and general characteristics of the excretion. Stuart's researches are also very unsatisfactory, and not of such a character as to lead to any conclusions worthy of reliance—no means of analysis other than the microscope having been employed.

The action of the disulphate of quinine upon the urine has, within a short period, been investigated by Ranke,<sup>3</sup> who found that the principal effect of its administration was to diminish the amount of uric acid excreted.

During a recent attack of intermittent fever of the tertian type, I had the

<sup>1</sup> Séméiotique des Urines, p. 286; and Traité de Chimie Pathologique, p. 345.

<sup>2</sup> Charleston Medical Journal and Review, May, 1857, p. 323.

<sup>3</sup> Medical Times and Gazette, May 30, 1857, p. 537.

opportunity of studying, in my own person, the effects produced by this disease on the physical and chemical qualities of the urine, and also of noticing the results ensuing from the administration of the disulphate of quinine.

There are many obvious advantages to the physiologist, and also to the science which he represents, in basing his conclusions, whenever practicable, on investigations instituted upon himself. He is assured of their correctness, and knows fully the conditions under which they are performed. On the contrary, when others (such at least as are most likely to come under his observation) are the subjects of his researches, he can never be certain that his directions have been complied with, or that he has not been otherwise deceived.

The investigations upon which this paper is based, being confined to one individual, are necessarily not such as to lead to general conclusions, and are only submitted as a slight contribution to our common stock of knowledge. Aside from their correctness, therefore, I have but little to claim for them.

The quantity, specific gravity, and general appearance of the urine were noted, and the amount of its urea, uric acid, free acid, chlorine, and phosphoric and sulphuric acids separately ascertained. The methods used in these determinations were the same as those employed in previous researches, and as elsewhere indicated.

The attack commenced at about 3½ o'clock P. M., on the 4th of January. The cold stage lasted about 35 minutes; the hot until near 10 P. M., when profuse perspiration ensued, and I fell asleep and did not awake till morning.

I was eating a hearty dinner when the paroxysm commenced. At 6½ P. M. I ate a little bread and butter and drank a cup of tea. At breakfast the following morning I ate as usual. As far as possible, my food was the same throughout the investigations, and my general mode of life was not materially changed.

At the commencement of the cold stage, the bladder was evacuated of its contents. At about 4½ P. M., it was again emptied. The quantity passed at this time amounted to 93.4 cubic centimetres, and had a specific gravity of 1016.35. It was of a pale straw colour, and deposited no sediment on standing. The reaction was feebly acid. Before going to sleep, I passed 283.9 cubic centimetres of urine, having a specific gravity of 1022.19. This was of high colour, strong acid reaction, and by morning had deposited a heavy lateritious sediment. On examining this with the microscope, a few crystals of uric acid were perceived.

In the morning, after rising, 495.3 cubic centimetres of urine were evacuated, the specific gravity of which was 1020.43. It was of high colour and strong acid reaction. A copious lateritious precipitate was thrown down after a short time; it consisted of urates and a little free uric acid.

For the whole period of twenty-four hours ending at 3½ P. M. on the 5th, the urine was as follows:—



Quantity . . . . .	1221.7 c. cm.
Specific gravity . . . . .	1020.06
Urea . . . . .	325.18 grains.
Uric acid . . . . .	28.39 "
Free acid . . . . .	39.40 "
Chlorine . . . . .	95.42 "
Phosphoric acid . . . . .	69.18 "
Sulphuric acid . . . . .	32.11 "

During the subsequent twenty-four hours of intermission, the urine was of the ensuing character:—

Quantity . . . . .	1650.4 c. cm.
Specific gravity . . . . .	1022.17
Urea . . . . .	480.37 grains.
Uric acid . . . . .	16.84 "
Free acid . . . . .	34.73 "
Chlorine . . . . .	114.58 "
Phosphoric acid . . . . .	52.95 "
Sulphuric acid . . . . .	38.14 "

From these records it is perceived that during the intermission there was an approach to the normal condition of the excretion under consideration. The quantity of urine, its specific gravity, and the amount of urea, chlorine, and sulphuric acid had increased, whilst at the same time the uric acid, free acid, and phosphoric acid had very considerably diminished.

The second paroxysm came on at about 4 o'clock P. M. on the 6th, and was of similar character to the first. At the termination of the chill, 104.5 cubic centimetres of urine were passed, the specific gravity of which was 1017.41. It was of a pale yellow colour, of feeble acid reaction, and remained clear. During the hot stage I evacuated 325.01 cubic centimetres of urine, of 1021.32 specific gravity, high colour, and strong acid reaction. After standing long enough to reduce its temperature sufficiently, a heavy precipitate of urates was thrown down, in which, with the microscope, a few crystals of uric acid were perceived. The urine passed after rising in the morning amounted to 518 cubic centimetres, was of 1022.04 specific gravity, and possessed the characteristics of that last described.

The following table shows the amount and character of the urine for the whole period of twenty-four hours ending at 3½ P. M. on the 7th:—

Quantity . . . . .	1387.2 c. cm.
Specific gravity . . . . .	1019.45
Urea . . . . .	300.16 grains.
Uric acid . . . . .	31.54 "
Free acid . . . . .	35.72 "
Chlorine . . . . .	108.11 "
Phosphoric acid . . . . .	72.95
Sulphuric acid . . . . .	41.76

At 4 o'clock P. M. on this day, I took ten grains of the disulphate of quinia, ten grains at 11 P. M., and the same quantity at 10 A. M. the following day. The paroxysm which would have ensued at about 4 P. M. was thus prevented.

The urine passed during this period of twenty-four hours was of the ordinary normal colour, and of tolerably strong acid reaction. No sediment was deposited on standing.

The following table exhibits its characters more in detail :—

Quantity . . . . .	1750.3 c. cm.
Specific gravity . . . . .	1024.67
Urea . . . . .	589.43 grains.
Uric acid . . . . .	13.79 "
Free acid . . . . .	27.54 "
Chlorine . . . . .	129.83 "
Phosphoric acid . . . . .	55.27 "
Sulphuric acid . . . . .	46.18 "

The presence of quinia was demonstrated by means of Herapath's test and viewing the crystals formed, with the microscope and by polarized light.

The effects resulting from the administration of the quinine are thus shown to have been well marked. The quantity of urine, its specific gravity, and the amount of urea, chlorine, and sulphuric acid were increased, whilst the uric acid, free acid, and phosphoric acid were, on the contrary, diminished.

From 3½ P. M. on this day to the same hour on the following day, I collected the urine evacuated, and submitted it to analysis. No quinine was taken during this period, and no paroxysm of the fever occurred.

Quantity . . . . .	1806.3 c. cm.
Specific gravity . . . . .	1024.81
Urea . . . . .	638.20 grains.
Uric acid . . . . .	12.71 "
Free acid . . . . .	25.80 "
Chlorine . . . . .	138.27 "
Phosphoric acid . . . . .	56.22 "
Sulphuric acid . . . . .	40.10 "

The above table exhibits pretty nearly the average condition of my urine in its normal state. It is seen that, notwithstanding no quinine was taken, the excretion maintained its general character of the previous day.

No more paroxysms ensued, and circumstances prevented me making at that time any further analysis of the urine.

The accompanying table, in which the several results obtained are collected together, will tend to facilitate reference :—



	1st day. Paroxysm.	2d day. Intermission.	3d day. Paroxysm.	4th day. Administra- tion of quinine.	5th day.
Quantity of urine	1221.7 c. cm.	1650.4 c. cm.	1387.2 c. cm.	1750.3 c. cm.	1806.3 c. cm.
Specific gravity	1020.06	1022.17	1019.45	1024.67	1024.81
Urea	325.18 grs.	480.37 grs.	300.16 grs.	589.43 grs.	638.20 grs.
Uric acid	28.39 "	16.84 "	31.54 "	13.79 "	12.71 "
Free acid	39.40 "	34.73 "	35.72 "	27.54 "	25.80 "
Chlorine	95.42 "	114.58 "	108.11 "	129.83 "	138.27 "
Phosphoric acid	69.18 "	52.95 "	72.95 "	55.27 "	56.22 "
Sulphuric acid	32.11 "	38.14 "	41.76 "	46.18 "	40.10 "

From these data it is perceived that, during an attack of intermittent fever, the uric acid and phosphoric acid are very much increased in amount, and the urea and chlorine greatly diminished. During the intermission, there is a close approach to the normal proportions of these constituents, but a subsequent paroxysm restores the former condition. The disulphate of quinia, however, produces a permanent impression on the character of the urine, and, with the return to the natural relations existing between the several substances entering into the composition of this excretion, the disease disappears.

There are several facts indicated by the foregoing researches, to which attention may be directed. Thus the increase in the amount of phosphoric acid eliminated during a paroxysm points strongly to the nervous origin of the disease. The excess in the amount of uric acid excreted, whilst at the same time the quantity of urea was so strikingly diminished, are facts of the highest importance, and, in connection with the circumstance that during the intermission, and after the administration of the quinine, the urea was increased and the uric acid diminished in quantity, show the close relation existing between these substances, and render more probable the theory that the former body is a product of the continued metamorphosis of the latter.

From so limited an array of facts as the preceding, no hypothesis in regard to the pathology of intermittent fever can be considered as tenable. If, however, the results of these investigations should be confirmed by subsequent observers, a great step will have been made towards a satisfactory theory of this disease, and a rational idea of the therapeutical action of the disulphate of quinine may be formed. The subject is, therefore, left for the present, with the hope that others will turn their attention to the furnishing of material for its elucidation.







